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#4

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RAW SEQUENCE LISTING   DATE: 03/18/2002
PATENT APPLICATION: US/09/903,171A   TIME: 15:37:23

Input Set : A:\510015-260.TXT
Output Set: N:\CRF3\03182002\I903171A.raw

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 4 <110> APPLICANT: De Robertis, Edward M.
 5       Bouwmeester, Tewis
 8 <120> TITLE OF INVENTION: Endoderm, Cardiac and Neural Inducing
 9       Factors
11 <130> FILE REFERENCE: 510015-260
13 <140> CURRENT APPLICATION NUMBER: US 09/903,171A
14 <141> CURRENT FILING DATE: 2001-07-11
16 <150> PRIOR APPLICATION NUMBER: US 60/020,150
17 <151> PRIOR FILING DATE: 1996-06-20
19 <160> NUMBER OF SEQ ID NOS: 10
21 <170> SOFTWARE: FastSEQ for Windows Version 3.0
23 <210> SEQ ID NO: 1
24 <211> LENGTH: 270
25 <212> TYPE: PRT
26 <213> ORGANISM: Xenopus
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32              20                  25                  30
33 Ser Leu Asn Ser Arg Gly Tyr Phe Arg Lys Glu Arg Gly Ala Arg Arg
34       35                  40                  45
35 Ser Lys Ile Leu Leu Val Asn Thr Lys Gly Leu Asp Glu Pro His Ile
36       50                  55                  60
37 Gly His Gly Asp Phe Gly Leu Val Ala Glu Leu Phe Asp Ser Thr Arg
38 65                  70                  75                  80
39 Thr His Thr Asn Arg Lys Glu Pro Asp Met Asn Lys Val Lys Leu Phe
40                  85                  90                  95
41 Ser Thr Val Ala His Gly Asn Lys Ser Ala Arg Arg Lys Ala Tyr Asn
42              100                 105                 110
43 Gly Ser Arg Arg Asn Ile Phe Ser Arg Arg Ser Phe Asp Lys Arg Asn
44          115                 120                 125
45 Thr Glu Val Thr Glu Lys Pro Gly Ala Lys Met Phe Trp Asn Asn Phe
46          130                 135                 140
47 Leu Val Lys Met Asn Gly Ala Pro Gln Asn Thr Ser His Gly Ser Lys
48 145                 150                 155                 160
49 Ala Gln Glu Ile Met Lys Glu Ala Cys Lys Thr Leu Pro Phe Thr Gln
50                  165                 170                 175
51 Asn Ile Val His Glu Asn Cys Asp Arg Met Val Ile Gln Asn Asn Leu
52              180                 185                 190
53 Cys Phe Gly Lys Cys Ile Ser Leu His Val Pro Asn Gln Gln Asp Arg
54          195                 200                 205
55 Arg Asn Thr Cys Ser His Cys Leu Pro Ser Lys Phe Thr Leu Asn His
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56      210                 215                 220
57  Leu Thr Leu Asn Cys Thr Gly Ser Lys Asn Val Val Lys Val Val Met
58  225                 230                 235                 240
59  Met Val Glu Glu Cys Thr Cys Glu Ala His Lys Ser Asn Phe His Gln
60                      245                 250                 255
61  Thr Ala Gln Phe Asn Met Asp Thr Ser Thr Thr Leu His His
62                      260                 265                 270
64  <210> SEQ ID NO: 2
65  <211> LENGTH: 1338
66  <212> TYPE: DNA
67  <213> ORGANISM: Xenopus
69  <400> SEQUENCE: 2
70  gaattcccag caagtcgctc agaaacactg cagggtctag atatcataca atgttactaa    60
71  atgtactcag gatctgtatt atcgtctgcc ttgtgaatga tggagcagga aaacactcag   120
72  aaggacgaga aaggacaaaa acatattcac ttaacagcag aggttacttc agaaaagaaa   180
73  gaggagcacg taggagcaag attctgctgg tgaatactaa aggtcttgat gaacccccaca  240
74  ttgggcatgg tgattttcgc ttagtagctg aactatttga ttccaccaga acacatacaa   300
75  acagaaaaga gccagacatg aacaaagtca agcttttctc aacagttgcc catggaaaca   360
76  aaagtgcaag aagaaaagct tacaatggtt ctagaaggaa tattttttcct cgccgttctt  420
77  ttgataaaag aaatacagag gttactgaaa agcctggtgc caagatgttc tggaacaatt   480
78  ttttggttaa aatgaatgga gccccacaga atacaagcca tggcagtaaa gcacaggaaa   540
79  taatgaaaga agcttgcaaa accttgtttt tcactcagaa tattgtacat gaaaactgtg   600
80  acaggatggt gatacagaac aatctgtgct ttggtaaatg catctctctc catgttccaa   660
81  atcagcaaga tcgacgaaat acttgttccc attgcttgcc gtccaaattt accctgaacc   720
82  acctgacgct gaattgtact ggatctaaga atgtagtaaa ggttgtcatg atggtagagg   780
83  aatgcacgtg tgaagctcat aagagcaact tccaccaaac tgcacagttt aacatggata   840
84  catctactac cctgcaccat taaaggactg ccatacagta tggaaatgcc ctttttgttgg  900
85  aatatttgtt acatactatg catctaaagc attatgttgc cttctatttc atataaccac   960
86  atggaataag gattgtatga attataatta acaaatggca ttttgtgtaa catgcaagat  1020
87  ctctgttcca tcagttgcaa gataaaaggc aatatttgtt tgactttttt tctacaaaat  1080
88  gaatacccaa atatatgata agataatggg gtcaaaactg ttaaggggta atgtaataat  1140
89  agggactaag tttgcccagg agcagtgacc cataacaacc aatcagcagg tatgatttac  1200
90  tggtcacctg tttaaaagca aacatcttat tggttgctat gggttactgc ttctgggcaa  1260
91  aatgtgtgcc tcatagggggg gttagtgtgt tgtgtactga ataaattgta tttatttcat  1320
92  tgttacaaaa aaaaaaaa                                                 1338
94  <210> SEQ ID NO: 3
95  <211> LENGTH: 318
96  <212> TYPE: PRT
97  <213> ORGANISM: Xenopus frazzled
99  <400> SEQUENCE: 3
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101  1               5                   10                  15
102  Gly Leu Ala Leu Leu Leu Leu Pro Asn Ala Tyr Cys Ala Ser Cys Glu
103                  20                  25                  30
104  Pro Val Arg Ile Pro Met Cys Lys Ser Met Pro Trp Asn Met Thr Lys
105              35                  40                  45
106  Met Pro Asn His Leu His His Ser Thr Gln Ala Asn Ala Ile Leu Ala
107      50                  55                  60
108  Ile Glu Gln Phe Glu Gly Leu Leu Thr Thr Glu Cys Ser Gln Asp Leu
```

```
109  65                    70                   75                    80
110  Leu Phe Phe Leu Cys Ala Met Tyr Ala Pro Ile Cys Thr Ile Asp Phe
111                    85                   90                    95
112  Gln His Glu Pro Ile Lys Pro Cys Lys Ser Val Cys Glu Arg Ala Arg
113                   100                  105                   110
114  Ala Gly Cys Glu Pro Ile Leu Ile Lys Tyr Arg His Thr Trp Pro Glu
115             115                  120                  125
116  Ser Leu Ala Cys Glu Glu Leu Pro Val Tyr Asp Arg Gly Val Cys Ile
117        130                  135                  140
118  Ser Pro Glu Ala Ile Val Thr Val Glu Gln Gly Thr Asp Ser Met Pro
119  145                  150                  155                   160
120  Asp Phe Ser Met Asp Ser Asn Asn Gly Asn Cys Gly Ser Gly Arg Glu
121                   165                  170                  175
122  His Cys Lys Cys Lys Pro Met Lys Ala Thr Gln Lys Thr Tyr Leu Lys
123             180                  185                  190
124  Asn Asn Tyr Asn Tyr Val Ile Arg Ala Lys Val Lys Glu Val Lys Val
125             195                  200                  205
126  Lys Cys His Asp Ala Thr Ala Ile Val Glu Val Lys Glu Ile Leu Lys
127        210                  215                  220
128  Ser Ser Leu Val Asn Ile Pro Lys Asp Thr Val Thr Leu Tyr Thr Asn
129  225                  230                  235                   240
130  Ser Gly Cys Leu Cys Pro Gln Leu Val Ala Asn Glu Glu Tyr Ile Ile
131             245                  250                  255
132  Met Gly Tyr Glu Asp Lys Glu Arg Thr Arg Leu Leu Leu Val Glu Gly
133             260                  265                  270
134  Ser Leu Ala Glu Lys Trp Arg Asp Arg Leu Ala Lys Lys Val Lys Arg
135        275                  280                  285
136  Trp Asp Gln Lys Leu Arg Arg Pro Arg Lys Ser Lys Asp Pro Val Ala
137        290                  295                  300
138  Pro Ile Pro Asn Lys Asn Ser Asn Ser Arg Gln Ala Arg Ser
139  305                  310                  315
141  <210> SEQ ID NO: 4
142  <211> LENGTH: 1875
143  <212> TYPE: DNA
144  <213> ORGANISM: Xenopus frazzled
146  <400> SEQUENCE: 4
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148  tgttgatttt gacacatgat tgattgcttt cagataggat tgaaggactt ggatttttat     120
149  ctaattctgc acttttaaat tatctgagta attgttcatt ttgtattgga tgggactaaa     180
150  gataaactta actccttgct tttgacttgc ccataaacta taaggtgggg tgagttgtag     240
151  ttgcttttac atgtgcccag attttccctg tattccctgt attccctcta aagtaagcct     300
152  acacatacag gttgggcaga ataacaatgt ctcgaacaag gaaagtggac tcattactgc     360
153  tactggccat acctggactg gcgcttctct tattacccaa tgcttactgt gcttcgtgtg     420
154  agcctgtgcg gatccccatg tgcaaatcta tgccatggaa catgaccaag atgcccaacc     480
155  atctccacca cagcactcaa gccaatgcca tcctggcaat tgaacagttt gaaggtttgc     540
156  tgaccactga atgtagccag gaccttttgt tctttctgtg tgccatgtat gcccccattt     600
157  gtaccatcga tttccagcat gaaccaatta agccttgcaa gtccgtgtgc gaaagggcca     660
158  gggccggctg tgagcccatt ctcataaagt accggcacac ttggccagag agcctggcat     720
159  gtgaagagct gcccgtatat gacagaggag tctgcatctc cccagaggct atcgtcacag     780
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160  tggaacaagg aacagattca atgccagact tctccatgga ttcaaacaat ggaaattgcg   840
161  gaagcggcag ggagcactgt aaatgcaagc ccatgaaggc aacccaaaag acgtatctca   900
162  agaataatta caattatgta atcagagcaa aagtgaaaga ggtgaaagtg aaatgccacg   960
163  acgcaacagc aattgtggaa gtaaaggaga ttctcaagtc ttccctagtg aacattccta  1020
164  aagacacagt gacactgtac accaactcag gctgcttgtg cccccagctt gttgccaatg  1080
165  aggaatacat aattatgggc tatgaagaca aagagcgtac caggcttcta ctagtggaag  1140
166  gatccttggc cgaaaaatgg agagatcgtc ttgctaagaa agtcaagcgc tgggatcaaa  1200
167  agcttcgacg tcccaggaaa agcaaagacc ccgtggctcc aattcccaac aaaaacagca  1260
168  attccagaca agcgcgtagt tagactaacg gaaaggtgta tggaaactct atggactttg  1320
169  aaactaagat ttgcattgtt ggaagagcaa aaaagaaatt gcactacagc acgttatatt  1380
170  ctattgttta ctacaagaag ctggtttagt tgattgtagt tctcctttcc ttcttttttt  1440
171  ttataactat atttgcacgt gttcccaggc aattgtttta ttcaacttcc agtgacagag  1500
172  cagtgactga atgtctcagc ctaaagaagc tcaattcatt tctgatcaac taatggtgac  1560
173  aagtgtttga tacttgggga aagtgaacta attgcaatgg taaatcagag aaaagttgac  1620
174  caatgttgct tttcctgtag atgaacaagt gagagatcac atttaaatga tgatcacttt  1680
175  ccatttaata ctttcagcag ttttagttag atgacatgta ggatgcacct aaatctaaat  1740
176  attttatcat aaatgaagag ctggtttaga ctgtatggtc actgttggga aggtaaatgc  1800
177  ctactttgtc aattctgttt taaaaattgc ctaaataaat attaagtcct aaataaaaaa  1860
178  aaaaaaaaaa aaaaa                                                    1875
180  <210> SEQ ID NO: 5
181  <211> LENGTH: 896
182  <212> TYPE: PRT
183  <213> ORGANISM: Xenopus
185  <400> SEQUENCE: 5
186  Met Leu Leu Leu Phe Arg Ala Ile Pro Met Leu Leu Leu Gly Leu Met
187  1               5                   10                  15
188  Val Leu Gln Thr Asp Cys Glu Ile Ala Gln Tyr Tyr Ile Asp Glu Glu
189              20                  25                  30
190  Glu Pro Pro Gly Thr Val Ile Ala Val Leu Ser Gln His Ser Ile Phe
191          35                  40                  45
192  Asn Thr Thr Asp Ile Pro Ala Thr Asn Phe Arg Leu Met Lys Gln Phe
193          50                  55                  60
194  Asn Asn Ser Leu Ile Gly Val Arg Glu Ser Asp Gly Gln Leu Ser Ile
195  65                  70                  75                  80
196  Met Glu Arg Ile Asp Arg Glu Gln Ile Cys Arg Gln Ser Leu His Cys
197              85                  90                  95
198  Asn Leu Ala Leu Asp Val Val Ser Phe Ser Lys Gly His Phe Lys Leu
199              100                 105                 110
200  Leu Asn Val Lys Val Glu Val Arg Asp Ile Asn Asp His Ser Pro His
201          115                 120                 125
202  Phe Pro Ser Glu Ile Met His Val Glu Val Ser Glu Ser Ser Ser Val
203          130                 135                 140
204  Gly Thr Arg Ile Pro Leu Glu Ile Ala Ile Asp Glu Asp Val Gly Ser
205  145                 150                 155                 160
206  Asn Ser Ile Gln Asn Phe Gln Ile Ser Asn Asn Ser His Phe Ser Ile
207              165                 170                 175
208  Asp Val Leu Thr Arg Ala Asp Gly Val Lys Tyr Ala Asp Leu Val Leu
209              180                 185                 190
210  Met Arg Glu Leu Asp Arg Glu Ile Gln Pro Thr Tyr Ile Met Glu Leu
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RAW SEQUENCE LISTING   DATE: 03/18/2002
PATENT APPLICATION: US/09/903,171A   TIME: 15:37:23

Input Set : A:\510015-260.TXT
Output Set: N:\CRF3\03182002\I903171A.raw

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211           195              200              205
212  Leu Ala Met Asp Gly Gly Val Pro Ser Leu Ser Gly Thr Ala Val Val
213      210              215              220
214  Asn Ile Arg Val Leu Asp Phe Asn Asp Asn Ser Pro Val Phe Glu Arg
215  225              230              235              240
216  Ser Thr Ile Ala Val Asp Leu Val Glu Asp Ala Pro Leu Gly Tyr Leu
217              245              250              255
218  Leu Leu Glu Leu His Ala Thr Asp Asp Asp Glu Gly Val Asn Gly Glu
219          260              265              270
220  Ile Val Tyr Gly Phe Ser Thr Leu Ala Ser Gln Glu Val Arg Gln Leu
221          275              280              285
222  Phe Lys Ile Asn Ser Arg Thr Gly Ser Val Thr Leu Glu Gly Gln Val
223      290              295              300
224  Asp Phe Glu Thr Lys Gln Thr Tyr Glu Phe Glu Val Gln Ala Gln Asp
225  305              310              315              320
226  Leu Gly Pro Asn Pro Leu Thr Ala Thr Cys Lys Val Thr Val His Ile
227              325              330              335
228  Leu Asp Val Asn Asp Asn Thr Pro Ala Ile Thr Ile Thr Pro Leu Thr
229          340              345              350
230  Thr Val Asn Ala Gly Val Ala Tyr Ile Pro Glu Thr Ala Thr Lys Glu
231          355              360              365
232  Asn Phe Ile Ala Leu Ile Ser Thr Thr Asp Arg Ala Ser Gly Ser Asn
233      370              375              380
234  Gly Gln Val Arg Cys Thr Leu Tyr Gly His Glu His Phe Lys Leu Gln
235  385              390              395              400
236  Gln Ala Tyr Glu Asp Ser Tyr Met Ile Val Thr Thr Ser Thr Leu Asp
237              405              410              415
238  Arg Glu Asn Ile Ala Ala Tyr Ser Leu Thr Val Val Ala Glu Asp Leu
239          420              425              430
240  Gly Phe Pro Ser Leu Lys Thr Lys Lys Tyr Tyr Thr Val Lys Val Ser
241      435              440              445
242  Asp Glu Asn Asp Asn Ala Pro Val Phe Ser Lys Pro Gln Tyr Glu Ala
243      450              455              460
244  Ser Ile Leu Glu Asn Asn Ala Pro Gly Ser Tyr Ile Thr Thr Val Ile
245  465              470              475              480
246  Ala Arg Asp Ser Asp Ser Asp Gln Asn Gly Lys Val Asn Tyr Arg Leu
247              485              490              495
248  Val Asp Ala Lys Val Met Gly Gln Ser Leu Thr Thr Phe Val Ser Leu
249          500              505              510
250  Asp Ala Asp Ser Gly Val Leu Arg Ala Val Arg Ser Leu Asp Tyr Glu
251      515              520              525
252  Lys Leu Lys Gln Leu Asp Phe Glu Ile Glu Ala Ala Asp Asn Gly Ile
253      530              535              540
254  Pro Gln Leu Ser Thr Arg Val Gln Leu Asn Leu Arg Ile Val Asp Gln
255  545              550              555              560
256  Asn Asp Asn Cys Pro Val Ile Thr Asn Pro Leu Leu Asn Asn Gly Ser
257              565              570              575
258  Gly Glu Val Leu Leu Pro Ile Ser Ala Pro Gln Asn Tyr Leu Val Phe
259          580              585              590
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VERIFICATION SUMMARY   DATE: 03/18/2002
PATENT APPLICATION: US/09/903,171A   TIME: 15:37:24

Input Set : A:\510015-260.TXT
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